CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
DEPARTMENT OF PESTICIDE REGULATION
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA
4,4-DIMETHYLOXAZOLIDINE AND 3,4,4-TRIMETHYLOXAZOLIDINE

Chemical Code # 002156 and 002157, DPN # 50262
SB 950 # 259 and 926
February 23, 2005

I. DATA GAP STATUS

Chronic toxicity, rat:	Data gap, no study submitted.
Subchronic, rat (dermal)	Data gap, inadequate study, no adverse systemic effect indicated
Chronic toxicity, dog:	Data gap, no study submitted
Oncogenicity, rat:	Data gap, no study submitted
Oncogenicity, mouse:	Data gap, no study submitted
Reproduction, rat:	Data gap, no study submitted.
Teratology, rat:	Data gap, no study submitted.
Teratology, rabbit:	No data gap, no adverse effect.
Gene mutation:	No data gap, possible adverse effect
Chromosome effects:	No data gap, possible adverse effect
DNA damage	No data gap, no adverse effect
Neurotoxicity:	Not required at this time

Toxicology one-liners are attached.
The registration for 3,4,4-trimethyloxazolidine has been withdrawn from California.
All record numbers through 114772 were examined.

** indicates an acceptable study.
Bold face indicates a possible adverse effect.
File name: T050223
Original: Kishiyama and Gee, February 23, 2005
There is a US EPA "Reregistration Eligibility Decision (RED)" on 4,4-Dimethyloxazolidine, dated August 1996. It rapidly hydrolyzes to formaldehyde and 2-amino-2-methyl-1-propanol.
4,4-Dimethyloxazolidine is an antimicrobial with non-food registrations only. There is no anticipated dietary exposure.

II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

These pages contain summaries only. Individual worksheets may contain additional effects.

COMBINED, RAT

No study submitted

CHRONIC TOXICITY, RAT

Subchronic:

015 114772 Pennisi, S. C. "Phase 3 Reformat of MRID No. 252955: Thirteen Week Subchronic Dermal Toxicity Study in Rats Amine CS-1135." (Avon Products, Inc., Study Project Code AT0156, April 24, 1980.) Amine CS-1135, 78% ai, was administered at doses of 0 (50-50 ethanol-water), 1.95, 19.5, and 195 mg ai/kg body weight, 5 days/week for a total of 67-68 days to 15 Sprague-Dawley rats/sex/group. Skin irritation was slight for the mid-dose group, but increased in incidence and severity for the high dose group. Dermal/systemic NOEL = 19.5 mg/kg/day. Reduced bodyweight gain for high dose females was attributed directly to skin irritation. Blood and serum changes were reported as not toxicologically significant. Note: This study was judged acceptable by the U.S.E.P.A. UNACCEPTABLE (insufficient information). Not upgradeable (no ophthalmology). (Kishiyama and Gee, 10/29/04).

The RED of US EPA lists another dermal study in the rat, which is not on file with the Department. The citation is: Allan, S., et al. (1994) "Thirteen-week dermal toxicity study in rats with 4,4-dimethyloxazolidine: Final report." Lab. No. TCC/3/931087:94/192A1. Huntingdon Research Center. The doses were 0, 1, 30 and 100 mg/kg/day, occluded for 6 hours, 5 days/week for 4 or 13 weeks. According to the summary in the RED, the systemic NOEL was $\geq$ 100 mg/kg/day. The dermal NOEL was 1 mg/kg/day based on microscopically observed changes in the treated skin (inflammation, ulceration, acanthosis). (Gee, 10/29/04)

CHRONIC TOXICITY, DOG

No study submitted

ONCOGENICITY, RAT

No study submitted

ONCOGENICITY, MOUSE

No study submitted

REPRODUCTION, RAT

No study submitted

TERATOLOGY, RAT

No study submitted

TERATOLOGY, RABBIT

** 014 114771 Arnold, K. S. "Dermal Teratology Study in Rabbits." (International Research and Development Corporation, IRDC 509-002, February 13, 1986.) Oxaban™ -A, purity not stated but assumed 78%, specific gravity 0.9832, was administered neat to the skin (shaven backs) of 16 mated New Zealand White female rabbits/group at doses of 0 (deionized water), 30, 100, and 300 mg/kg/day for 6 hours/day on gestation days 7 through 19. Volumes were 0.0305, 0.1017 and 0.3051 ml/kg of undiluted material as supplied. Thrashing in the cage immediately after dosing occurred in 1, 5 and 4 does treated with 30, 100 and 300 mg/kg, respectively, on days 18 and/or 19 of gestation. Maternal NOEL $\leq$ 30 mg/kg/day (skin irritation). Developmental NOEL $\geq$300 mg/kg/day. ACCEPTABLE (Kishiyama and Gee, 10/29/04).

GENE MUTATION

**** 004 - 028365** "L5178Y TK +/- Mouse Lymphoma Mutagenesis Assay" (Kirby, P. E., study director, Microbiological Associates, Bethesda, MD, Study No. T1840-701001, January 24, 1983.) 4,4-Dimethyloxazolidine (aqueous solution, lot 6178-29) was assayed at 16 concentrations ranging from 0.0024 to 0.032 µl/ml without metabolic activation and from 0.01 to 0.1 µl/ml with S9 Mix for mutagenicity using mouse lymphoma cells. Exposure was for 4 hours followed by a 2-day expression period. There were triplicate plates for mutagenicity and for viability from a single culture per concentration. The five highest concentrations without activation (0.01 to 0.032 :l/ml) and the two highest activated concentrations (0.075 and 0.1 :l/ml) induced mutation frequencies that were significantly higher than solvent controls. Positive controls were functional**. Possible adverse effect.** ACCEPTABLE (with minor variances). (D. Shimer and J. Wong, 6/27/85).

002 982994 Ames Mutagenicity Test of Bioban CS-1135 on *Salmonella typhimurium* (1 Page summary). Angus Chemical Company. Summary states that the study was negative for CS-1135. UNACCEPTABLE (insufficient information/no data). (D. Shimer and J. Wong, 6/27/85).

Haworth, S. R., Lawlor, T. E., Smith, J. K. et al. (1980) "Salmonella/mammalian-microsome plate incorporation mutagenesis assay." Study no. 035-201-430-1. Unpublished study prepared by EG&G Mason Research Institute, submitted by International Minerals and Chemical Corp., Terre Haute, Ind. Not on file.

Haworth, S. R., Lawlor, T. E., Smith, J. K. et al. (1980) "Salmonella/mammalian-microsome plate incorporation mutagenesis assay." Study no. 035-201-431-1. Unpublished study prepared by EG&G Mason Research Institute, submitted by International Minerals and Chemical Corp., Terre Haute, Ind. Not on file.

CHROMOSOME EFFECTS

**** 004 028364** "Cytogenicity Study – Chinese Hamster Ovary (CHO) Cells *In Vitro*."

(Thilagar, A., study director, Microbiological Associates Bethesda, MD Study No. T1840.338, December 21, 1982.) 4,4-Dimethyloxazolidine solution (lot 6178-29) was assayed at concentrations of 0 (water), and 0.02 to 0.15 µl/ml without activation and 0.07 to 0.5 µl/ml with metabolic activation (S9 Mix) using Chinese hamster (CHO) ovary cells. Exposure was for 4 hours followed by a 16-hour further incubation. Mitotic cells were collected by mitotic shake-off for evaluation. Fifty metaphase cells per concentration were scored from three concentrations with and without activation. Both with and without activation, the % of cells with aberrations and the number per cell were significantly increased. **Possible adverse effect**. ACCEPTABLE (with minor variances). (D. Shimer and J. Wong, 6/27/85).

Asquith, J. (1984) Cytogenic analysis of the bone marrow of rats treated with HP 60/83 (Oxaban-A or Bioban CS-1135." Lab project no SR374, prepared by Toxicol Laboratories, Ltd. Not on file.

DNA DAMAGE

** 014 114770 Enninga, I.C. "Evaluation of the DNA Repair Inducing Ability of Oxaban™ - A (Bioban™CS-1135)." (RCC NOTOX, The Netherlands, RCC Project No. 020327, February 13, 1990.) Oxaban™, purity 78%, was evaluated for DNA repair inducing ability at concentrations of 0, 10, 33, 100, 333, 1000, 3300 and 5000 µg/ml in Experiment #1 and at 0, 1.0, 3.3, 10, 33, 100, 333 and 1000 µg/ml in Experiment #2, using male Wistar rat hepatocytes, exposed for 18 hours with triplicate coverslips per concentration. The highest concentrations were toxic in both experiments (5000 and 1000 ug/ml). Unscheduled DNA synthesis was measured by autoradiography with 50 cells scored per coverslip. No evidence of mutagenic activity was reported. ACCEPTABLE. (Kishiyama and Gee, 10/29/04).

The US EPA RED lists another study that is not on file with the Department. The citation is: Enniga, I. (1989) "Micronucleus test in bone marrow cells of the mouse with Oxaban-A (Bioban CS-1135)." Lab no. 0112522, RCC Notox. The summary in the RED stated that the test was negative at 500 mg/kg but the PCE/NCE ratio was decreased at 72 hours. (Gee, 10/29/04)

NEUROTOXICITY

Not required at this time.